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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/878,131	06/08/2001	Guofan Hong	Lee113	1143

7590 04/30/2004  
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EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT PAPER NUMBER

1637

DATE MAILED: 04/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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**Office Action Summary****Application No.**

09/878,131

**Applicant(s)**

HONG ET AL.

**Examiner**

Suryaprabha Chunduru

**Art Unit**

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**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --****Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 January 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-11 and 18-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 18-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

**DETAILED ACTION**

1. Applicants' response to the office action filed on January 23, 2004 has been entered and considered.

2. Claims 1-11, 18-35 are pending.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-11, 18-35 are rejected under 35 U.S.C. 102 (b) as being anticipated by Hong et al. (USPN. 5,834,253).

With reference to the instant claims 9-11, 22-23, 30-31, Hong et al. teach a method for extending an oligonucleotide primer annealed to a DNA template (double-stranded or single-stranded DNA) for direct cycle sequencing (classic Sanger one-step reaction) at temperatures between 45 C and 65 C and a melting temperature below about 80 C (see column 5, lines 1-17, column 12, lines 1-67, column 13, lines 1-7, column 18, lines 60-67, column 19, lines 1-49, column 20, lines 1-21) comprising (i) mixing a template with a primer (sequencing primer), four standard ddNTP terminators or their analogs, a DNA polymerase which has proof-reading 3'-5' exonuclease activity, such that the DNA polymerase functions to excise mismatched nucleotides from 3'-terminus of the DNA strand at a faster rate than the rate at which the DNA polymerase functions to remove nucleotides matched correctly with nucleotides of the template under conditions that DNA polymerase repeatedly extends the primer (see column 5, lines 2-12); (ii)

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effecting cycle primer extension reaction at temperature below 80 C (see column 5, lines 13, column 12, lines 8, 50-55, column 19, lines 3-5).

With regard to claims 9-11, 22-23, 30-31, Hong et al. also teach that the method comprises (i) DNA polymerase selected from *Bacillus stearothermophilus* (see column 5, lines 14-17, column 12, lines 14-24); Bst is functional within the temperature range between 25 C and 75 C (see column 12, lines 50-55, column 20, lines 4-12);

With regard to claims 22-23, 30-31, Hong et al. also teach use of fluorescent dye labeled nucleotides (see column 13, lines 1-7);

With regard to claims 22-23, 30-31, Hong et al. also teach that said DNA polymerase reduces the innate selective discrimination against the incorporation of nucleotide analogs such as ddNTPs, dITP and 7-deaza-dGTP (see column 12, lines 56-64);

With reference to the instant claims 18-21, 24-27, 32-35, Hong et al. teach that the method comprises DNA polymerase having homology (99-100%) to the instant claimed SEQ ID Nos. 1-4 (see sequence listing of patent '253 and attached sequence alignment);

With regard to claims 9-10, 22, 28, 30, Hong et al. disclose that the method comprises about 10% (w/v) glycerol, (see column 19, lines 6-11);

Thus the disclosure of Hong et al. meets the limitations in the instant claims.

### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker (USPN. 5,712,124) in view of Hong et al. (USPN. 5,834,253).

With regard to claim 1-4, Walker teaches a method for extending an oligonucleotide primer or a pair of oligonucleotide primers using enzymatic cycle primer extension reaction (SDA) (see column 10, lines 4-67, column 11, lines 1-25) at temperatures between about 45<sup>0</sup> C and about 65<sup>0</sup> C and a melting temperature of about 70<sup>0</sup> C (see column 10, lines 17-34), wherein the method comprises (i) the step of mixing a template with a primer or a pair of primers and a thermostable DNA polymerase (see column 10, lines 40-64), wherein, the DNA polymerase lacks 5'-3' exonuclease activity, is selected from the group consisting of *Bacillus stearothermophilus* (Bst) DNA polymerase (column 10, lines 3-16, lines 47-52) and extending the primer at cycle reaction temperature fluctuates between about 70<sup>0</sup> C and about 37<sup>0</sup> C (see column 10, lines 20-28). Walker also teaches that the reaction mixture can also contain glycerol, ethyl glycol (see column 10, lines 28-34).

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With regard to claims 5-6, Walker also teaches that the method further comprises repeating the cycle primer extension, in the presence of a forward and a reverse primer to a template (see column 10, lines 58-64);

With regard to claim 7, Walker teaches that the forward and reverse primers have varying lengths (see column 12, lines 4-5).

However Walker did not specifically teach the proofreading 3'-5' exonuclease activity of Bst which functions to excise mismatched nucleotides from the 3' terminus of the DNA strand at a faster rate than the rate at which the DNA polymerase functions, and direct cycle sequencing using dideoxynucleotide terminators.

With reference to the instant claims 1-8, Hong et al. teach a method for replicating or amplification and sequencing DNA using a DNA polymerase having proofreading 3'-5' exonuclease activity and has the capability of removing mismatched nucleotides from the 3'-terminus of a newly formed DNA strand at a faster rate (see column 4, lines 42-67, column 5, lines 1-20) Hong et al. also teach that the method comprises sequencing cycle sequencing method (see column 12, lines 1-8, column 18, lines 60-67, column 19, lines 1-45) (i) about 10% (w/v) glycerol, (see column 19, lines 6-11); (ii) DNA polymerase selected from *Bacillus stearothermophilus* (see column 12, lines 14-24); method also comprises nucleotide analogs, such as ddNTPs, dITP (see column 12, lines 1-8).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of single cycle primer extension as taught by Walker with the proofreading 3'-5' exonuclease activity of Bst polymerase as taught by Hong et al. to

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achieve an expected benefit of developing a sensitive method for detecting the sequence of a target nucleic acid because Hong et al. taught the advantage of using Bst which has the proofreading 3'-5' exonuclease activity in addition to be suited work at low temperature (temperature range between 25<sup>0</sup> C and 75<sup>0</sup> C) reaction conditions (see column 19, lines 46-49, column 20, lines 1-12). An ordinary practitioner would have been motivated to combine the method of single cycle primer extension as taught by Walker with advantage of using Bst polymerase as taught by Hong et al. because inclusion of the proofreading property of Bst in the method of Walker would result in a sensitive method with high specificity to correct the misincorporation of mismatched nucleotides.

#### **Response to arguments**

5. Applicants' response to the office action (Paper No. 20) is fully considered and found persuasive.
6. With regard to the rejection made in the previous office action under 35 USC 103(a) over Kurn et al. in view of Mian et al. et al. , Applicants' arguments are fully considered and the rejection is withdrawn in view of the arguments and new grounds of rejections.
7. With regard to the rejection made in the previous office action under 35 USC 103(a) over Hong et al. in view of Mian et al., Applicants' arguments are fully considered and the rejection is withdrawn in view of the arguments and new grounds of rejections.

#### **Conclusion**

No claims are allowable.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-


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0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Suryaprabha Chunduru  
April 22, 2004

  
JEFFREY FREDMAN  
PRIMARY EXAMINER